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Junttila, Ilkka S.

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# Challenges in investigation of diabetes-related aviation fatalities—an analysis of 1491 subsequent aviation fatalities in USA during 2011–2016

Ilkka S. Junttila<sup>1,2</sup> · Alpo Vuorio<sup>3,4</sup> · Bruce Budowle<sup>5</sup> · Tanja Laukkala<sup>6</sup> · Antti Sajantila<sup>4</sup>

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## Abstract

Diabetes mellitus (DM) could cause pilot incapacitation and result in aviation fatalities. The mechanisms could be directly as a consequence of acute hypoglycemia/subacute diabetic ketoacidosis (DKA) or indirectly as an acute cardiovascular event by contributing to the development of atherosclerosis in coronary or carotid and cerebral arteries. In this study, DM-related fatal flight accidents in the US National Transport Bureau's database between years 2011–2016 were analyzed with special emphasis on postmortem (PM) glucose levels and correlation of toxicological reports with anamnestic information on DM. Additionally, autopsy results on coronary arteries were reviewed. In 43 out of 1491 (~3%) fatal accidents pilots had DM. Postmortem glucose or glycated hemoglobin percentage (Hb1Ac) was measured in 12 of the 43 cases; while antidiabetic medication was found in 14 of the cases (only two of the cases had both glucose measurements and medication). With the increasing prevalence of DM, a possibility of pilot incapacitation due to DM or complications of DM should be actively studied, even if no anamnestic information of DM was available. While PM hypoglycemia is difficult to assess, we propose a systematic investigation based on measurement of glucose, Hb1Ac%, and ketone bodies, and documentation of atherosclerotic lesions in major arteries to identify or rule out DM as a cause of pilot incapacitation.

**Keywords** Pilot incapacitation · Fatal flight accident · Accident investigation · Diabetes · Glucose measurement · Diabetic ketoacidose · Hypoglycemia · Hyperglycemia

## Abbreviations

FAA	Federal aviation administration
AME	Aviation medical examiner
ICAO	International civil aviation organization
CAA	Civil aviation authority

NTSB	National transportation safety board
DKA	Diabetic ketoacidosis
HbA1c	Glycated hemoglobin
AMI	Acute myocardial infarction
CNS	Central nervous system
PM	Postmortem
CO	Carbon monoxide

Ilkka S. Junttila and Alpo Vuorio contributed equally to this work.

✉ Antti Sajantila  
antti.sajantila@helsinki.fi

<sup>1</sup> Faculty of Medicine and Life Sciences, University of Tampere, Tampere, Finland

<sup>2</sup> Finlab Laboratories, Tampere, Finland

<sup>3</sup> Mehiläinen Airport Health Centre, Vantaa, Finland

<sup>4</sup> Department of Forensic Medicine, University of Helsinki, Helsinki, Finland

<sup>5</sup> Center for Human Identification, University of North Texas Health Science Center, 3500 Camp, Bowie Blvd., Fort Worth, TX 76107, USA

<sup>6</sup> Mehiläinen Kielotie Health Centre, Vantaa, Finland

## Introduction

Roughly 30.3 million adults in the USA have diabetes (diabetes mellitus, DM) and the overall prevalence of DM is 9.4%. Strikingly, of these individuals, 7.2 million are not aware they have DM (~24% of all diabetics) (<http://www.diabetes.org/diabetes-basics/statistics/>). In aviation, DM does not necessarily prevent a pilot from obtaining a license to fly. In the UK, the UK Civil Aviation Authority (CAA) may permit, according to recent practice, a class I medical certificate (required for all pilots involved in commercial aviation) to commercial pilots with type I DM upon careful monitoring of

blood glucose level [1]. In contrast in the USA, insulin-treated DM remains an absolute disqualifying condition for obtaining a class I medical certificate; however, private pilots may obtain a specific waiver to obtain a certificate to fly [2]. As for aviation safety, since ~24% of people with DM are unaware of their disease (<http://www.diabetes.org/diabetes-basics/statistics/>), screening of pilots for undiagnosed DM should be a requisite. The screening necessity is of particular importance given an increasing aging of the general population (note that prevalence of DM in individuals 65 years and older is 25.2%; <http://www.diabetes.org/diabetes-basics/statistics/>) and that in the USA currently only very limited checkups for aging pilots are required [3].

Pilot incapacitation due to DM-related causes may occur gradually or suddenly. Typical forms of sudden incapacitation are hypoglycemia, in which loss of consciousness is due to lack of glucose in the central nervous system (CNS) [4] and ischemia-induced cardiac arrhythmias. Furthermore, DM-associated hypoglycemia can subject a person to cardiac arrhythmias, especially with type 2 diabetes (DM2) [5]. DM also increases the risk of cardiovascular disease two- to five-fold [6], which increases the risk of a pilot to become suddenly incapacitated due to acute myocardial infarction (AMI) or cardiac arrhythmia induced by AMI. In addition to coronary atherosclerosis being more common in diabetic individuals, the prognosis of diabetics with coronary atherosclerosis is poorer than in non-diabetics [7, 8]. In fact, a person with diagnosed DM2 without previous AMI has a similar risk of developing AMI than a non-diabetic with previous AMI [9]. Finally, DM also directly increases the risk of a stroke [10].

Incapacitation may also occur gradually due to hyperglycemia. In hyperglycemia, incapacitation occurs via glucagon induction and subsequent rise in blood glucose level, as well as fatty acid release from adipose tissue. If glucose balance is not corrected, this process eventually leads to diabetic ketoacidosis (DKA). Sudden pilot incapacitation due to hypoglycemia is difficult to demonstrate, since reliable blood glucose level or insulin measurement postmortem (PM) is challenging; but gradual incapacitation caused by DKA can be readily addressed [11].

Hypoglycemia, as a possible cause of pilot incapacitation, is considered in flight accidents involving pilots with DM, but the task is hampered by rapid depletion of glucose (and insulin) PM [12]. A pilot's medical history available for accident investigators is often incomplete, but by combining data from a pilot's medical records and PM toxicological and biochemical analyses estimations can be made of the short- and long-term glucose balance of DM treatment prior to an accident. In aviation fatalities biochemical PM investigation should include the analysis of long-term blood glucose balance (percent of glycated hemoglobin, HbA1c) as well as urine and vitreous glucose levels [12–14]. New tools for investigating DM-related pH imbalance, for example ketone bodies, have

also been added to PM investigations [11, 15], while on the basis of methodological development [16] and systematic case evaluation adding HbA1c measurement into all routine PM evaluations of carbohydrate metabolism disturbance was recently suggested [16].

In this study, we analyze how DM was addressed in fatal flight accident final reports in the USA between 2011 and 2016 to better understand the challenges posed by DM-related conditions (hypoglycemia, hyperglycemia, DKA, and microvascular diseases).

## Materials and methods

Systematic analysis of fatal flight accidents in the USA between 1/1/2011–14/7/2017 with DM as an underlining factor for the incidents was performed on August 15, 2017 in the National Transportation Safety Board Aviation (NTSB) database ([https://www.nts.gov/\\_layouts/ntsb.aviation/index.aspx](https://www.nts.gov/_layouts/ntsb.aviation/index.aspx)). The search word used was “diabetes”. The search returned 45 cases of 1491 fatal flight accidents during this period, of which 2 were not linked to DM (one case included discussion on management of DM after stroke and the other one discussed treatment of diabetes insipidus). PM reports were reviewed with special focus on analysis of body fluid glucose and/or HbA1c as a read-out for imbalance of DM treatment. In addition, whether DM was reported to the Federal Aviation Administration (FAA) in the latest aeromedical assessment(s) before the accident flight was assessed.

## Results

### Anamnestic evidence of DM in the accident reports

Of the 43 cases identified, FAA was informed in 18 (42%) cases that the pilot had DM, and in the latest aeromedical assessment, 17 (40%) of the cases DM were not reported. In the remaining eight (19%) cases, it was unclear if FAA was aware of pilots' DM (Table 1) (N.B. the percent of cases, 42% + 40% + 19%, is 101% due to the percent round up of numbers). Interestingly, in 37 (86%) cases, there was

**Table 1** Anamnestic knowledge of DM diagnosis of pilots by primary health care (GP) or FAA in 43 fatal flight accidents involving pilots with DM in the USA between 2011 and 2016. (N.B. the percent of cases, 42% + 40% + 19%, is 101% due to the percent round up of numbers)

Knowledge of DM	GP no. of cases (%)	FAA no. of cases (%)
Informed	37 (86)	18 (42)
Not informed	2 (5)	17 (40)
Not known	4 (9)	8 (19)

indication that the general practitioner (GP) or primary care doctor was aware of the DM diagnosis, in four (9%) cases, it was unclear if the primary health care provider was aware of the DM and in two cases, the primary care doctor was not aware of the DM diagnosis.

## Postmortem laboratory data

### Toxicology reports

The toxicology reports of the accident investigation reports were reviewed with special emphasis on evidence of DM. In 14 (33%) of the 43 cases, PM toxicology provided evidence of DM, i.e., glipizide alone ( $n = 5$ ), pioglitazone alone ( $n = 5$ ), glyburide ( $n = 1$ ), sitagliptin ( $n = 2$ ), combination of glipizide and pioglitazone ( $n = 1$ ). The general characteristics of the accidents in these 14 cases are shown in Table 2. Of these 14 cases, diagnosis of DM was reported to FAA in 9 cases, in 3 cases, known DM was not reported and in 2 cases, it was unclear whether FAA was notified of the pilots' DM.

The toxicology reports indicated that many of the pilots used other personal medications, and in some cases, they used illicit drugs or medications not allowed in flying. For other PM toxicological analysis, carbon monoxide (CO) was analyzed in 15 cases (all cases were negative) and not analyzed in 28 cases. Ethanol was analyzed in 27 cases (20 negative). Six postmortem toxicology tests for ethanol were positive, but in these cases, ethanol was from sources other than ingestion. In one case, it was impossible to deduce whether the ethanol was from ingestion or other sources. Of the 16 cases where ethanol was not analyzed PM, seven cases had elevated PM glucose values. In addition, five of these 16 cases had antidiabetic medication in PM toxicology.

**Table 2** Summary of postmortem-identified antidiabetic medications of pilots in DM diabetes-related fatal flight accidents in the USA between 2011 and 2016. Altogether, 43 accidents were found; in 14 cases, postmortem toxicology of the pilots was positive for antidiabetic medication. Number of lives lost in these accidents is indicated. *M*, male; *No*, number

DM medication in toxicology	Pilot age, sex, and accident year	No. of lost lives in the accident
Glipizide	60 M, 2011	1
	65 M, 2011	1
	56 M, 2012	1
	69 M, 2012	1
	68 M, 2016	1
	53 M, 2011	1
Pioglitazone	63 M 2012	1
	62 M, 2012	1
	74 M, 2013	1
	44 M, 2013	2
	73 M, 2014	1
	63 M, 2015*	2
Glyburide	56 M, 2016	1
Sitagliptin	79 M, 2012**	1

\*flight student, \*\*flight instructor

### Glucose analysis

Since PM glucose level analysis in urine samples has been in routine use in aviation accident investigations in the USA since 1998 or for long-term glucose balance analysis (HbA1c) since mid-2001 [17], the accident investigation final reports between 2011 and 2016 were reviewed to analyze how systematic was PM evaluation of glucose balance (Table 3). Quantitative information on any type of glucose information (vitreous, blood, urine) was reported in only 11 cases; in one report urine glucose was “detected” but not quantitated. Average percent of blood HbA1c ( $n = 9$ ) was 7.9% (4.8–10.3%), average urine glucose ( $n = 11$ ) was 1271 mg/dl (12–3000 mg/dl) and average vitreous glucose ( $n = 8$ ) was 42 mg/dl (0–149 mg/dl). No information on possible ketone body measurements was available. Two hundred thirty-four milligram per deciliter [18] or 180 mg/dl [19] have been suggested as cutoff values for fatal antemortem (AM) hyperglycemia in vitreous fluid. Practically, any trace of glucose in the vitreous fluid is likely an indication of antemortem hyperglycemia [20]. For urine PM glucose measurements, specifying cutoff values for evaluating AM glucose balance from PM urine samples is challenging, and the urine glucose measurement should primarily be used to confirm vitreous findings [21–23].

## Discussion

Between 2011 and 2016, 43 flight accidents related to DM in the USA were discovered in the NTSB aviation database (out of 1491 accidents; ~3%). As a reference, Chaturvedi et al. performed a search of elevated vitreous and/or urine glucose in fatal flight accidents between 1998 and 2005 in the USA for 2487 deceased pilots, and they found 43 had elevated glucose

**Table 3** Available postmortem glucose metabolism measurements from diabetes DM-related flight accidents between 2011 and 2016 in the USA. Where available, the source of the blood sample for HbA1c measurement is indicated in parentheses. *N/A* data not available, *M* male, Blood source: *C* cavity, *H* heart, *F* femoral artery

Pilot age, sex, and accident year	Blood HbA1c %	Urine glucose (mg/dl)	Vitreous glucose (mg/dl)
63 M, 2011	4.8% (C)	3000	Not detected
63 M, 2012	N/A	Detected	Not detected
51 M, 2012	N/A	2460	N/A
79 M, 2012**	8.7%	1150	N/A
58 M, 2013	7.0% (H)	1949	149
58 M, 2013	9.2% (C)	484	N/A
51 M, 2013	10.3% (C)	1668	46
56 M, 2013	8.6% (F)	2514	82
73 M, 2014	6.1%	12	N/A
47 M, 2014	N/A	248	51
57 M, 2014	7.4%	135	Not detected
80 M, 2015	9.0%	366	8

\*\*flight instructor

levels (1.7%) [17]. Altogether, 58 lives were lost in the reviewed accidents here; the mean age of pilots (all male) was 62.4 (range 28–83 years), the median age was 63 years. In addition, in these accidents eight persons were severely injured, and one person suffered minor injuries. In 25 cases, health-related issues were not indicated as affecting the accident according to the accident final report; while in 18 cases, health of the pilot was either contributing to the accident or it was not possible to rule out that a health issue contributed to the accident. Autopsies revealed that in nine cases, the pilots had coronary atherosclerosis. In cases, where coronary atherosclerotic occlusion (%) was indicated in the autopsy report ( $n = 7$ ), the area of coronary artery occlusion was  $> 75\%$ . In other cases, the occlusion was indicated by description as “severe” ( $n = 1$ ) or “mild” ( $n = 1$ ). In six additional cases, atherosclerosis was present, but either its severity was not reported in the autopsy or the information was based on medical records.

Fatal flight accidents are investigated with a standardized protocol (ICAO annex 13) [24]. The protocol aims at investigating all contributory explanations for the accident and to identify the actual cause for an accident so that future accidents may be prevented. The medical condition of a pilot is always a critical part of such an investigation. With the increasing incidence of DM2, its role as a possible cause or contributing factor in an accident needs to be considered. In 2013, global prevalence of DM (both DM1 and DM2) was estimated to be 382 million people and in 2035, it is estimated to be 592 million people, with DM2 representing  $\sim 85\%$  of all DM cases [25]. Both the risk for AMI and for stroke are elevated in diabetic individuals [6, 9, 10]. In addition, older individuals with DM are at substantial risk of acute cardiovascular complications [26], which underlines the importance of health reviews of aging pilots especially those with DM.

The role of insulin-treated DM is relatively low as a cause of accidents involving pilots carrying a third-class medical

certificate, a certificate required to obtain a private pilot license in the USA [2]. This estimation is based on the analysis of 1500 waivers for insulin-treated DM approved by FAA, which did not indicate increased risk for fatal accidents between 1997 and 2014 for pilots with DM [2]. The overall accident rate for pilots with a waiver for insulin was 7.0 for 100,000 flight hours, while an estimate for all third-class pilots was exactly the same (7.0/100,000 flight hours) [2]. This finding would suggest that insulin-treated DM may not add risk for an accident. However, this conclusion may underestimate the role of DM, due to the fact that hypoglycemia that might affect the accident is difficult to address in PM diagnostics. Interestingly, the prevalence of DM (DM1 and DM2) in the USA is 9.4% (<http://www.diabetes.org/diabetes-basics/statistics/>) while pilots with DM in fatal flight accidents in the USA the prevalence was  $\sim 3\%$ , which would also suggest that DM was not increasing the risk for fatal accidents since prevalence among diabetic pilots in accidents is actually lower than DM in the general population. Various explanations could account for this difference. First, the lack of information flow of the pilots' DM to the aviation authority (FAA) may result in an underestimation of the number of diabetic pilots (Table 1) and thus could discourage the search for DM in accident review. Retrospectively, in cases studied herein, FAA was informed in only 43% of the cases that the pilots had DM. Second, medical screening of pilots may remove diabetics with more severe DM-related complications as pilot candidates. Third, the medical screening (for HbA1c and diabetic complications) combined with more regular doctor visits for pilots with DM might select pilots with DM that are overall more healthier than non-diabetic pilots. Fourth, the difficulty in measuring postmortem hyperglycemia and particularly hypoglycemia might underestimate the number of diabetes-related accidents. Fifth, a combination of these factors could be involved.



Interestingly, antidiabetic medication in the toxicology reports and elevated glucose in the body fluids correlated only in two cases. This could be due to a good balance of DM treatment. Those individuals not using the DM medication (either for not knowing they did have DM or for lack of compliance) would have elevated glucose levels. However, it is also possible that antidiabetic medication subjects one to hypoglycemia. Another common cause of hypoglycemia could be ethanol particularly combined with antidiabetic medication [27]. In this study, of the 16 cases where ethanol was not analyzed PM, seven cases had elevated PM glucose values which leaves open the theoretical possibility of ethanol-induced hypoglycemia in nine cases. One of these individuals with unclear ethanol status and antidiabetic medication had elevated glucose levels PM. In four cases with antidiabetic medication, PM without ethanol assessment hypoglycemia status remain unknown, but possible.

In a diabetic individual glucose, HbA1c% and ketone body levels are measured to determine the balance of DM treatment. In clinics, blood (and urine) glucose levels can be easily measured. However, when treating diabetic patients, long-term glucose levels are important for patient evaluation [28]. HbA1c% provides a reliable measure of blood glucose level over a period of several weeks (4–8 weeks), while it does not catch acute hypoglycemia. In clinics, HbA1c measurement is usually combined with a measurement of blood glucose level (either fasting or non-fasting) as well as serum ketone bodies and acidosis (serum bicarbonate) [4, 28]. In the routine postmortem investigation, DM as a primary or underlining cause of death is difficult to diagnose due to lack of specific macroscopic and microscopic findings. Also, PM glucose analysis is not feasible due to rapid glucose metabolism (glycolysis) into lactate [21]. However, using the recently developed biochemical analyses, and alternative matrices (such as vitreous humor and urine), fatal DM-related ketoacidosis is readily diagnosed, even in cases of no medical history of DM or cadavers with advanced postmortem changes [22, 29, 30]. Recently Palmieri discussed the caveats on using a single measurement as a definitive indication of dysregulation of glucose metabolism [31]; single measurement of glucose metabolism from any PM sample is likely unreliable. HbA1c and vitreous glucose measurements are used to assess glucose balance. The measurement of urine glucose can be supportive of the results obtained in vitreous fluid but if the urine is the only sample available, the significance of the measurement results should be carefully estimated [12–14]. It is clear that more sophisticated measurement tools of glucose balance will help in analyzing AM glucose balance in postmortem analysis; one candidate approach could be 1,5-anhydro-d-glucitol, which has shown promise in identifying AM diabetic coma in postmortem analysis [32]. In the USA, vitreous fluid and urine glucose analyses were

implemented as routine tests for flight accident investigations in the beginning of 1998, and blood HbA1c testing was implemented in the middle of 2001 [17]. One difficulty in assessing DM as a cause of pilot incapacitation in aviation accidents is the high energy forces associated with the accidents which make it difficult to obtain samples (body fluids) for analysis. Another critical feature in PM investigation related to DM is the status of coronary arteries and major CNS-arteries in context of atherosclerosis as a complication of DM. Finally, an accident investigation needs to take into account what factor(s) medication(s) may play in pilot incapacitation. Insulin and oral DM medication are a risk factor for hypoglycemia, and other simultaneous medications via various mechanisms may increase the hypoglycemic effect of oral DM medication [33]. Thus, pilots' medical records for prescriptive or over the counter medications, as well as toxicological report findings, need to be reviewed from the perspective of medication-induced hypoglycemia. Recently, analysis of exogenous insulin has become possible from postmortem samples [30, 31, 34, 35] which can also be added to aviation fatality investigation when hypoglycemia due to insulin use is suspected.

Multidrug use is a common finding in the realm of medicolegal autopsies [36, 37] and it is also challenge for fatal aviation accident investigations, as well as to AMEs and pilots' general practitioners. In cases reviewed herein, the median age of pilots during the accident was 63. Recently, 13% of US general aviation pilots over 70 years involved in a fatal accident were shown to have used three or more medications during the accident as indicated by the toxicology findings, with antihistamines and antidepressants the most frequently discovered substances [3].

Hypoglycemia, as a cause of sudden pilot incapacitation, is currently practically nearly impossible to address. Hyperglycemia and insulin deficiency-related DKA as cause of gradual pilot incapacitation should be investigated more extensively. Overall, given the high prevalence of DM, especially in the aging population, and the lack of disclosure of DM to FAA indicated in the study herein, glucose measurements, accompanied by measurement of ketone bodies (acetone, acetoacetate,  $\beta$ -hydroxybutyrate), should be a part of a standard investigation in an aviation fatality during the postmortem investigation of the pilot.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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